PDBP
Parkinson's Disease Biomarkers Program

* Required fields

Adverse Events

*Name of Site: _____

*Type of Visit: _____
e.g. Screening, Baseline, 6 months, 12 months, 18 months, 24 months, 30 months, 36 months, 42 months, 48 months, 54 months, 60 months.

*Date of Visit: _____

*GUID: _____

*Age of Subject (years and months): _____

Subject ID: _____

Has the participant/subject had any adverse events during the study? ☐ Yes ☐ No ☐ Unknown

Record diagnoses (if known) or signs/symptoms the participant/subject experienced during the study that qualify as adverse events.

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Adverse Event	Start Date (mm/dd/yyyy)	End Date (mm/dd/yyyy)	Severity	Relatedness	Action Taken with Study Intervention	Other Action Taken	Outcome	Serious Adverse Event?
	___/___ /20___	___/___ /20___	☐ Mild ☐ Moderate ☐ Severe ☐ Life-threatening/ Disabling ☐ Fatal/Death	☐ Unrelated ☐ Unlikely ☐ Probable ☐ Possible ☐ Definite	☐ None ☐ Study Intervention Interrupted ☐ Study Intervention Discontinued ☐ Study Intervention Modified	☐ None ☐ Non-Study Treatment Required	☐ Recovered/Resolved ☐ Recovered/Resolved With Sequelae ☐ Recovering/Resolving ☐ Not Recovered/Not Resolved ☐ Fatal ☐ Unknown	☐ No ☐ Yes *
	___/___ /20___	___/___ /20___	☐ Mild ☐ Moderate ☐ Severe ☐ Life-threatening/ Disabling ☐ Fatal/Death	☐ Unrelated ☐ Unlikely ☐ Probable ☐ Possible ☐ Definite	☐ None ☐ Study Intervention Interrupted ☐ Study Intervention Discontinued ☐ Study Intervention Modified	☐ None ☐ Non-Study Treatment Required	☐ Recovered/Resolved ☐ Recovered/Resolved With Sequelae ☐ Recovering/Resolving ☐ Not Recovered/Not Resolved ☐ Fatal ☐ Unknown	☐ No ☐ Yes *
	___/___ /20___	___/___ /20___	☐ Mild ☐ Moderate ☐ Severe ☐ Life-threatening/ Disabling ☐ Fatal/Death	☐ Unrelated ☐ Unlikely ☐ Probable ☐ Possible ☐ Definite	☐ None ☐ Study Intervention Interrupted ☐ Study Intervention Discontinued ☐ Study Intervention Modified	☐ None ☐ Non-Study Treatment Required	☐ Recovered/Resolved ☐ Recovered/Resolved With Sequelae ☐ Recovering/Resolving ☐ Not Recovered/Not Resolved ☐ Fatal ☐ Unknown	☐ No ☐ Yes *
	___/___ /20___	___/___ /20___	☐ Mild ☐ Moderate ☐ Severe ☐ Life-threatening/ Disabling ☐ Fatal/Death	☐ Unrelated ☐ Unlikely ☐ Probable ☐ Possible ☐ Definite	☐ None ☐ Study Intervention Interrupted ☐ Study Intervention Discontinued ☐ Study Intervention Modified	☐ None ☐ Non-Study Treatment Required	☐ Recovered/Resolved ☐ Recovered/Resolved With Sequelae ☐ Recovering/Resolving ☐ Not Recovered/Not Resolved ☐ Fatal ☐ Unknown	☐ No ☐ Yes *

** Yes should be answered when the adverse event results in death, is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.*

Adverse Events CRF Module Instructions

General Instructions

ADVERSE EVENTS

Adverse events (AEs) document medical events that occur to a participant/subject once enrolled in a study. AEs are the construct through which the safety of an intervention is recorded and assessed during a study. Typical AE descriptors include event start date, severity, relatedness, outcome, and an indication of whether the event is serious.

RECORDING ADVERSE EVENTS

All AEs, both serious and non serious, regardless of relationship to the study intervention, should be recorded on the AE case report form (CRF). AE data should be collected from the time the informed consent form is signed through the duration of the clinical investigation. Standard medical terminology should be used when recording AEs. Furthermore, it is recommended that studies that plan to submit data to regulatory authorities should code their AE data using the Medical Dictionary for Regulatory Activities (MedDRA) or Common Terminology Criteria for Adverse Events (CTCAE).

SERIOUS ADVERSE EVENTS

A serious adverse event is (SAE) defined as any untoward medical occurrence that at any dose results in one of the following outcomes: Death; A life-threatening adverse drug experience; Results in inpatient hospitalization or prolongation of existing hospitalization; A persistent or significant disability/incapacity; A congenital anomaly/birth defect.

Important medical events that may not result in death, be life threatening, or require hospitalization may be considered a serious adverse drug event when, based upon appropriate medical judgment, they may jeopardize the participant/subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsion that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

If an event is documented as serious, then a separate SAE Report form must completed. For studies under a Food and Drug Administration (FDA) Investigational New Drug (IND) application, a 3500A is completed and submitted as an expedited report, if the event is also unexpected and related to the study intervention. Because the data collected for an SAE are descriptive and beyond the scope of a study, the SAE information is usually kept in a separate file. In addition to the SAE descriptors, it is useful to track when the SAE is sent to the Institutional Review Board (IRB), sponsor, Food and Drug Administration (FDA), and Data Safety Monitoring Board (DSMB) and responses received.

In some neurological studies, there has been confusion over the relationship between a study endpoint (e.g., myocardial infarction) and an SAE. The AE may be heart attack, described as mild. However, since it resulted in a hospitalization, it is coded as “serious” (SAE). The event may also be a study endpoint that is captured on the SAE form and sent for adjudication. This process would be tracked but the information collected is generally beyond the study scope and is not captured on study case report forms nor entered into the study data management system.

Specific Instructions

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

- **Any Adverse Events?** – Choose one. If answered YES, at least one AE must be recorded.
- **AE Description** – Any untoward medical occurrence in a study participant/subject that does not necessarily have a causal relationship with the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease

temporally associated with the use of a study intervention or study procedure, whether or not related to the study intervention or procedure. Each AE should be listed on a separate line. Any worsening of a baseline condition or reoccurrence of a baseline condition that had previously ended for a time should be listed as an AE. Events, such as nausea and vomiting are considered two events, and therefore should be listed on separate lines. A participant/subject may experience an unexpected AE. An unexpected adverse reaction has a nature or severity of which is not consistent with the study intervention description (e.g. Investigator's Brochure for an unapproved investigational product or package insert/summary of product characteristics for an approved product). The unexpected AE must be reported, whether related to the study intervention or not, with as much detail as is available. See the Data Dictionary for additional information on coding the adverse events using either the Common Terminology Criteria for Adverse Events (CTCAE) or the Medical Dictionary for Regulatory Activities (MedDRA).

- **Start Date and Time**– Record the date (and time) the adverse event started. The date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in the format acceptable to the study database. If a previously recorded AE worsens, a new record should be created with a new start date/time. There should be no AE start date prior to the date of the informed consent. Any AE that started prior to the informed consent date belongs instead in the medical history. If an item recorded on the medical history worsens during the study, the date of the worsening is entered as an AE with the start date/time as the date/time the condition worsened.
- **End Date and Time**– Record the date (and time) the adverse event stopped or worsened. The date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in the format acceptable to the study database. If an AE worsens, record an end date/time and create a new AE record with a new start date/time and severity.
- **Severity** – Choose the one severity that best describes the investigator's assessment of the intensity of the AE. The five severity grades are from the Common Terminology Criteria for Adverse Events v4.0 (CTCAE). Severe events interrupt the participant's/subject's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating. Consequently, a change in severity may constitute a new reportable AE. Severity is not synonymous with seriousness. A severe rash is not likely to be an SAE. Likewise, a severe headache is not necessarily an SAE. However, mild chest pain may result in a day's hospitalization and thus is an SAE. It is helpful to define the severity categories in the protocol or Manual of Operations to obtain consistency in reporting across sites.
- **Relatedness** – Choose one. Record the investigator's assessment of the degree of "relatedness" of the AE to the study intervention. Before beginning a study, definitions for each of the relatedness responses should be supplied.
- **Action Taken with Study Intervention**– Choose one. This CDE is only appropriate for clinical trials and should be removed from the CRF if a study does not have an intervention.
- **Other Action Taken** – Choose one. If treatment was required, then the corresponding treatment needs to be recorded on the Prior and Concomitant Medications CRF.
- **Outcome** – Choose one. The outcome of an AE may not be captured at the visit during which it was first reported, but must be captured to provide a complete picture of the event. Entering the outcome of an AE may be deferred until the AE is resolved, or the participant/subject completes the study. For AEs that have not resolved at the time of a study visit, the outcome should be marked as "unresolved" on the AE case report form.
- **Serious** – Choose either Yes or No. This question should only be answered YES if the outcome of the AE results in at least one of the following: death; a life-threatening adverse drug experience; results in inpatient hospitalization or prolongation of existing hospitalization; a persistent or significant disability/incapacity; or a congenital anomaly/birth defect. If an AE is serious, this provides a trigger that

additional information must be provided by the site investigator. The site investigator then completes a Serious Adverse Event (SAE) form. Additionally, the site institution and/or IRB may also have an SAE form and procedures for reporting SAEs.